

Environmental Fate of Fipronil

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Revised March 5, 2007

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I. Introduction

This document reviews the environmental fate of fipronil (5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfinyl]-1*H*-pyrazole-3-carbonitrile); Figure 1). Fipronil is a phenylpyrazole insecticide (Tingle et al., 2003) discovered by Rhône-Poulenc Ag Company (now Bayer CropScience) in 1987, introduced in 1993 (The Pesticide Manual, 2000), and registered in the U.S. in 1996 (Ware, 2000). The insecticide controls a broad spectrum of insects such as cockroaches, mosquito, locust, ticks, and fleas at both larval and adult stages (Chanton et al., 2001; Aajoud et al., 2003). Fipronil is effective, at low field application rates, against insects that are resistant to pyrethroids, organophosphates, and carbamate insecticides (Bobe et al., 1997). For instance, Stevens et al. (1998) found that fipronil applied to rice seed at 12.5 g active ingredient (a.i.)/ha is more efficacious than malathion at 300 g a.i./ha and provides protection against chironomid insects for 9-14 days after sowing rice seed. Fipronil can be formulated as solid (e.g., insect bait; White, 1998), liquid spray, or as a granular product (e.g., turf application; U.S. EPA, 1996) and these influence its environmental fate. Ngim and Crosby (2001) found that the granular product of fipronil was most persistent of its formulations in water, half life ($t_{1/2}$) was 125 hours, and soil ($t_{1/2}$ = 438 hours). Fipronil is the active ingredient in Frontline®, Termidor® and Top Spot®. The insecticide is classified as a chiral pesticide and released to the environment as a racemic mixture. Approximately 119,000 lbs of fipronil was used in California in 2006, primarily for structural pest control (CDPR, 2006). The insecticide is not registered for production agricultural use in the state of California.

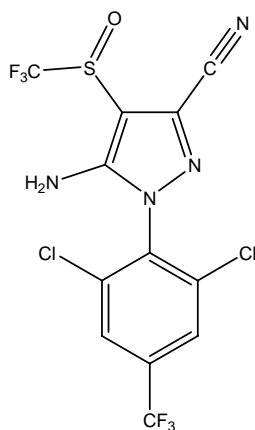


Fig. 1. Chemical structure of fipronil.

II. Chemistry

A. Physical-chemical properties

Fipronil is low to moderately soluble in water, prefers lipophilic (organic) matrices such as lipids, oils, lignin, proteins, and organic solvents, and is stable at room temperatures (Aajoud et al., 2003; Table 1). It has a low to moderate affinity for organic carbon environments (e.g., soils) as well as biota ($\log K_{ow}$ is 3.9-4.1) and falls between highly insoluble pesticides (e.g., DDT K_{ow} is 6.2) and soluble ones such as atrazine (K_{ow} is 2.6; Demcheck and Skrobialowski, 2003). According to Table 1, fipronil is denser than water, not expected to become volatile, is degraded through photolysis, susceptible to hydrolysis under alkaline, but not, acidic conditions, and has varying microbial degradation times depending on the condition of the soil environment (i.e., anaerobic or aerobic).

Table 1. Physical-chemical properties of fipronil. All parameters are at 25°C unless specified.

Chemical Abstract Service registry number (CAS #) ¹		120068-37-3
Molecular weight (g/mol) ¹		473.2
Solubility ¹	Water (mg/L; pH = 5)	1.90
	Water (mg/L; pH = 9)	2.40
	Hexane (mg/L)	28.0
	Toluene (mg/L)	3000
Melting point (°C) ¹		200-201
Density (g/mL 20°C) ¹		1.48-1.63
Vapor pressure (mPa; calculated) ⁶		3.7×10^{-4}
Henry's constant (m ³ ·atm/mol; experimental) ²		6.60×10^{-6}
Henry's constant (m ³ ·atm/mol; calculated) ⁶		8.50×10^{-10}
Octanol-water partition coefficient (Log K _{ow}) ⁶		3.50
Organic carbon normalized partition coefficient (averaged K _{oc}) ³		825
Aqueous photolysis (days; pH = 5) ⁶		0.33
Hydrolysis half-life (days) ⁴	pH = 5.5	>100
	pH = 7.0	>100
	pH = 9.0	32.08
	pH = 10	4.75
	pH = 11	0.45 (11 hours)
	pH = 12	0.1 (2.4 hours)
Aerobic soil half-life (days) ⁵		188
Anaerobic soil half-life (days) ²	Dry flowable formulation	19.3-22.2
	Granular formation	18.3
Anaerobic water half-life (days) ¹	Dry flowable formulation	0.92-2.83
	Granular formation	5.20

¹ The Pesticide Manual, 2000; ² Ngim and Crosby, 2001; ³ Ying and Kookana, 2001; ⁴ Bobe et al., 1998b; ⁵ Ying and Kookana, 2002; ⁶ Rhône-Poulenc Ag Company, 1998.

B. Mode of Action

Fipronil is a “new generation” insecticide as its mode of action does not follow the common biochemical pathways of pyrethroids (sodium channel blockers), organophosphates, and carbamate (cholinesterase inhibitors) which are classical insecticides to which some insects have developed resistance (Aajoud et al., 2003). Cole et al. (1993) found that fipronil interferes with the γ -aminobutyric acid (GABA)-gated channels; fipronil disrupts normal nerve influx transmission (e.g., passage of chloride ions) by targeting the GABA-gated chloride channel and

at sufficient doses, causes excessive neural excitation, severe paralysis, and insect death (Aajoud et al., 2003; Bobe et al., 1998a; Gant et al., 1998). Fipronil demonstrates a selective toxicity toward insects (LC_{50} can be low as 24.8 nM or $\sim 11.7 \mu\text{g/L}$) by having a tighter binding affinity toward the GABA-regulated chloride channels of insects than the mammalian GABA receptors (Hainzl et al., 1996).

III. Environmental Fate

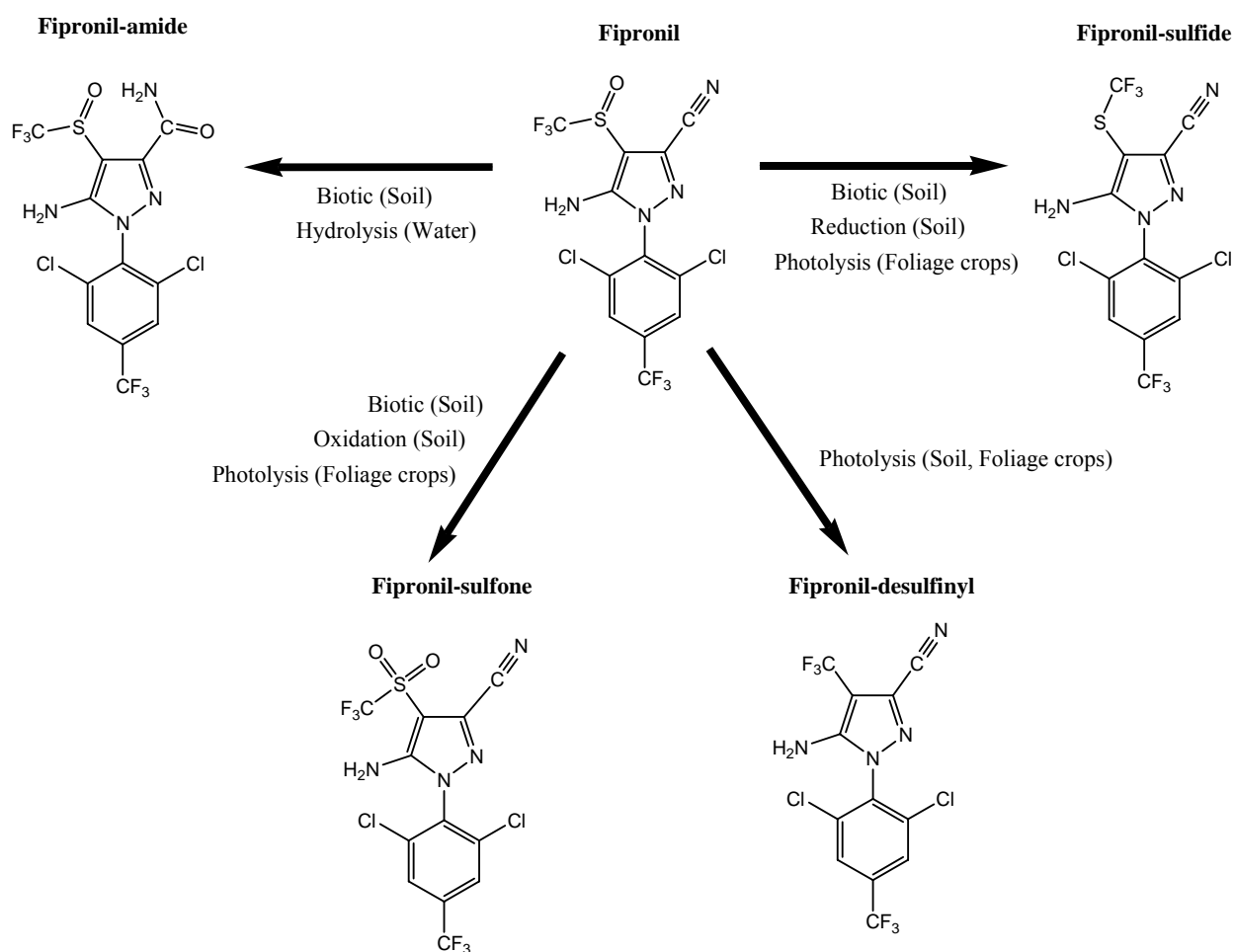


Figure 2. The dissipation of fipronil to fipronil-sulfide, fipronil-desulfinyl, fipronil-sulfone, and fipronil-amide via reduction, oxidation, photolysis, hydrolysis, and biotic reaction mechanisms, respectively. Bracketed texts indicate the medium in which the reaction is expected to take place.

A. Soil

Several studies have examined the behavior of fipronil distribution in soil. Bobe et al. (1997) has shown that adsorption increased as the OM content in soil increased from 0.1 to 6.5%. A similar observation was noted by Ying and Kookana (2001) in eight different Australian soils. The K_{oc} values ranged from 542-1176 for fipronil (average 825 ± 214) depending on the Australian soil and indicates low to moderate sorption (Table 1). Similar K_{oc} values were found after sorption studies of fipronil with British and French loam soils; 427-1248 (Rhône-Poulenc Ag Company, 1998). These results indicate that fipronil is relatively mobile in soils. Leaching studies confirm the mobility of fipronil in soils since results showed that 31-37% of surface soil-applied fipronil moved into the 6-12 cm layer (Rhône-Poulenc Ag Company, 1998).

Calculated $t_{1/2}$ for fipronil in the 0-10 cm soil layer was approximately 36 hours (Bobe et al., 1998a). However, it could be much longer depending on the soil. For instance, the $t_{1/2}$ in loam soil was found to be 34 days (Tingle et al., 2003) while in sandy loam, it ranged from 30 to 194 days (Rhône-Poulenc Ag Company, 1998).

The dissipation of fipronil and its breakdown products, under sub-Saharan soil conditions, has been studied by Bobe et al. (1998a). Fipronil and its degradates (Figure 2) did not move beyond the 10 cm soil depth, except for fipronil-amide which is the most polar and water soluble of the breakdown products. The study noted that the leaching of fipronil-amide coincided with a rainfall event. Dissipation of the fipronil in the environment is a result of exposure to sunlight to produce fipronil-desulfinyl, reductive processes in soils lead to fipronil-sulfide, oxidation yields fipronil-sulfone, and hydrolysis produces fipronil-amide (Figure 2). The $t_{1/2}$ of the fipronil and its breakdown products in soil revealed they are persistent; degradation ranges from 111-350 days. The sorption K_{oc} of fipronil-sulfide and fipronil-desulfinyl to several Australian soils was higher

than the parent compound and ranged from 1479-7159 and 669-3976, respectively (Ying and Kookana, 2001). Similar results were reported elsewhere; K_{oc} for fipronil-sulfide ranged from 1695-5621 in sediment and loam soils while for fipronil-sulfone and fipronil-amide it ranged from 1447-6745 and 96-203 in the same soils. Additionally, the major soil photo-degradation product, fipronil-desulfinyl, had a slightly larger sorption affinity for soils than the parent compound with K_{oc} 's ranging from 1150-1498 (Rhône-Poulenc Ag Company, 1998).

The metabolites of fipronil have been detected in river bed sediments (Mermentau River) that is within a rice agriculture region in Louisiana according to Demcheck and Skrobialowski (2003). Fipronil-sulfide was the predominant metabolite and found at concentrations that ranged from 0.636-24.8 $\mu\text{g/kg}$ in the river bed sediment while the photolytic byproduct (fipronil-desulfinyl) concentrations ranged from 0.55-7.01 $\mu\text{g/kg}$. Fipronil-sulfone was also detected (up to 10.5 $\mu\text{g/kg}$) in the river bed sediment. Additionally, there was an increasing trend in the concentration of the degradates with downstream river bed sediment sampling sites. In general, fipronil behavior in soil reveals that it has low to moderate sorption and is mobile in soils. Fipronil and its metabolites have been detected in several water bodies in the U.S. at low concentrations.

B. Water

U.S. Geological Survey monitoring work that shows, since 2002, the presence of fipronil, its sulfone, and sulfide degradates in low ppb ($\mu\text{g/L}$) concentrations in urban creeks of the Sacramento and San Joaquin Rivers of California (Table 2). Also, in Louisiana, where fipronil was used to control the rice water weevil in rice agriculture, fipronil and three of its degradates (fipronil-sulfone, sulfide, and desulfinyl) were detected in several locations in the Mermentau river basin (Demcheck and Skrobialowski, 2003). Throughout the U.S., fipronil and its

metabolites have been detected in several water bodies in urban and agricultural areas, but at low concentrations (Table 2). The highest recorded concentration for fipronil was found in Louisiana at 0.117 µg/L while for fipronil-sulfone, fipronil-sulfide, fipronil-desulfinyl, and fipronil-amide it was 0.038 µg/L (Colorado), 0.015 µg/L (Louisiana), 0.158 µg/L (California), and 0.011 µg/L (Louisiana), respectively. The Louisiana detections were made in surface water from mainly agricultural areas. However, Demcheck and Skrobialowski (2003) reported much higher levels, as high as 5.29 µg/L fipronil, from a Louisiana rice field study. Additionally, the same study found that fipronil and its aerobic degradation products (fipronil-desulfinyl and fipronil-sulfone) were detected at maximum concentrations in March and April; months that coincide with the release of rice field water. It is important to note that although fipronil is primarily used for agriculture, domestic urban use is substantial (Table 2) and accounts for about half of all detection types.

The dissipation of fipronil in an aquatic system (Figure 2) over three months revealed two transformations of the parent compound; photo-dependent and hydrolysis of the sulfide and nitrile side chains bound to the heterocyclic ring (Aajoud et al., 2003). Under anaerobic conditions such as rice field soils, fipronil degrades slowly in water. The $t_{1/2}$ on average is 123 days, much longer than any aerobic soil system where fipronil and fipronil-desulfinyl $t_{1/2}$ is only 5 days (Tingle et al., 2003; Rhône-Poulenc Ag Company, 1998). Two major metabolites were produced under these water conditions: fipronil-sulfide and fipronil-amide.

Table 2. Detection of fipronil and its degradates in the U.S. according to the U.S. Geological Survey @.

State	Fipronil			Fipronil-sulfone			Fipronil-sulfide		
	Type of Land use	Detections *	Concentration Range (µg/L)	Type of Land use	Detections *	Concentration Range (µg/L)	Type of Land use	Detections *	Concentration Range (µg/L)
Alabama	Urban	9	0.007-0.017	Urban	4	0.004-0.008	Urban	5	0.005-0.013
California	Urban	37	0.004-0.080	Urban	30	0.005-0.022	Urban	31	0.005-0.014
	Agriculture	1		Mixed	2		Mixed	3	
	Mixed	7							
Colorado	Agriculture	1	0.003-0.050	Agriculture	1	0.038	Agriculture	1	0.008
	Mixed	2							
Connecticut	Urban	4	0.006-0.008	Urban	1	0.005	Urban	3	0.005-0.008
Georgia	Urban	26	0.001-0.026	Urban	10	0.005-0.008	Urban	11	0.003-0.009
	Mixed	39		Mixed	3		Mixed	8	
Iowa	Mixed	1	0.007	Agriculture	1	0.003	Mixed	1	0.007
Illinois	Urban	14	0.005-0.0191	Urban	1	0.005-0.010	Urban	3	0.003-0.008
	Agriculture	4		Agriculture	3		Agriculture	3	
	Mixed	12		Mixed	1		Mixed	2	
Indiana	Urban	6	0.002-0.020	Agriculture	4	0.002-0.007	Agriculture	1	0.003-0.005
	Agriculture	23					Mixed	2	
	Mixed	14							
Louisiana	Urban	8	0.002-0.117	Urban	8	0.002-0.016	Urban	8	0.004-0.015
	Agriculture	7		Agriculture	12		Agriculture	16	
	Mixed	11		Mixed	13		Mixed	13	
Massachusetts	Urban	1	0.002-0.011	Mixed	2	0.005-0.008	Mixed	2	0.007-0.008
	Mixed	7							

@ U.S. Geological Survey NAWQA data warehouse, 2006; * since 2003.

Table 2 (continued). Detection of fipronil and its degradates in the U.S. according to the U.S. Geological Survey[@].

State	Fipronil-desulfinyl			Fipronil-amide		
	Type of Land use	Detections *	Concentration Range (µg/L)	Type of Land use	Detections *	Concentration Range (µg/L)
Alabama	Urban	6	0.002-0.008	Urban	3	0.002-0.006
	Mixed	2		Agriculture	1	
California	Urban	36	0.005-0.158	Urban	12	0.002-0.009
	Mixed	8		Mixed	4	
Colorado	Urban	1	0.003-0.006	-	-	-
	Agriculture	1				
	Mixed	2				
Connecticut	Urban	3	0.002-0.005	-	-	-
Georgia	Urban	11	0.002-0.008	Urban	7	0.004-0.008
	Agriculture	2		Mixed	3	
	Mixed	13				
Iowa	Mixed	1	0.005	-	-	-
Illinois	Urban	5	0.002-0.007	Agriculture	1	0.009
	Agriculture	3				
	Mixed	3				
Indiana	Urban	1	0.002-0.008	-	-	-
	Agriculture	4				
	Mixed	9				
Louisiana	Urban	8	0.004-0.037	Urban	5	0.002-0.011
	Agriculture	12		Agriculture	11	
	Mixed	10		Mixed	10	
Massachusetts	Mixed	2	0.006-0.007	Mixed	2	0.006-0.008

[@] U.S. Geological Survey NAWQA data warehouse, 2006; * since 2003.

C. Air

The volatilization of fipronil (Table 1) into air was confirmed to be slow by Ngim and Crosby (2001); Henry's constant was experimentally determined to be $6.60 \times 10^{-6} \text{ m}^3 \text{ atm/mol}$. In the same study, the fipronil-desulfinyl breakdown product was found to be nonvolatile from water (Ngim and Crosby, 2001). These findings suggest that fipronil does not readily volatilize and thus will not be found in the air. However, drift during its spray application may still occur.

IV. Degradation

A. Abiotic

Fipronil degrades rapidly by means of reduction, hydrolysis, oxidation, and photolysis to form four major metabolites (Figure 2; Bobe et al., 1998b). The four degradates include fipronil-sulfide, which is a product of reduction in soil, an fipronil-amide, a product of hydrolysis in water and soil, fipronil-sulfone, from oxidation in soil, and fipronil-desulfinyl, a result of photolysis (Bobe et al., 1997). The parent compound and each metabolite have unique dissipation kinetics which are discussed below.

B. Photolysis

Photolytic exposure of fipronil (pH 5.5 and representative of Sahelian soil conditions) led to rapid first-order degradation kinetics with a calculated $t_{1/2}$ of 4.1 hours (Bobe et al., 1998b). Similar results were obtained in another study: 0.33 days or 7.92 hours (Rhône-Poulenc Ag Company, 1998). Thus, the effects of sunlight on fipronil have been proposed to be a major route for its degradation.

The photo-degradation of fipronil has been studied further by several groups. For instance, Hainzl and Casida (1996), and Bobe et al. (1998b) found four photoproducts (Figure 3).

According to Hainzl and Casida (1996), the formation of fipronil-desulfinyl is accelerated three-fold by adding 1% hydrogen peroxide. Ngim and Crosby (2001) confirmed that the presence of hydrogen peroxide leads to shorter dissipation time; $t_{1/2}$ was 0.87-4.51 hours compared to 7.97-9.42 hours for the parent compound in the absence of hydrogen peroxide. The increase is primarily due to the generation of hydroxyl radicals as a result of irradiation. Fipronil-desulfinyl was found to be the major photo-degradation product after fipronil application to corn, pea, and pear crops (Hainzl and Casida, 1996) and thus, is proposed to be the primary persistent residue on foliage-treated crops. This byproduct had a half-life of 41-55 days and was also the most abundant among all the degradation products (Ying and Kookana, 2002). No polar metabolites were found according to Hainzl and Casida (1996).

Photo-degradation has been found to be inversely proportional to sorption (Bobe et al., 1997). Water phase fipronil photolysis experiments were extended to solid phase (soil) by Bobe et al. (1998b). They found that photolytic degradation was slower in soil as compared in water as a result of the “light-shielding” effect discussed by Oliver et al. (1979). Additionally, the rate of degradation was found to depend on the nature of the soil and correlate with the Freundlich adsorption coefficient (K_F or sorption capacity). These factors can contribute to reducing the dissipation of fipronil in soil.

C. Hydrolysis

The degradation of fipronil in aqueous solution in the absence of light at 22°C at different pH was studied by Bobe et al. (1998b). The insecticide was stable in acid (pH 5.5) and neutral (pH 7.0) pH solutions; 80% remained after 100 days. However, under alkaline conditions (pH 9-12), degradation increased with pH and followed pseudo-first-order transformation kinetics

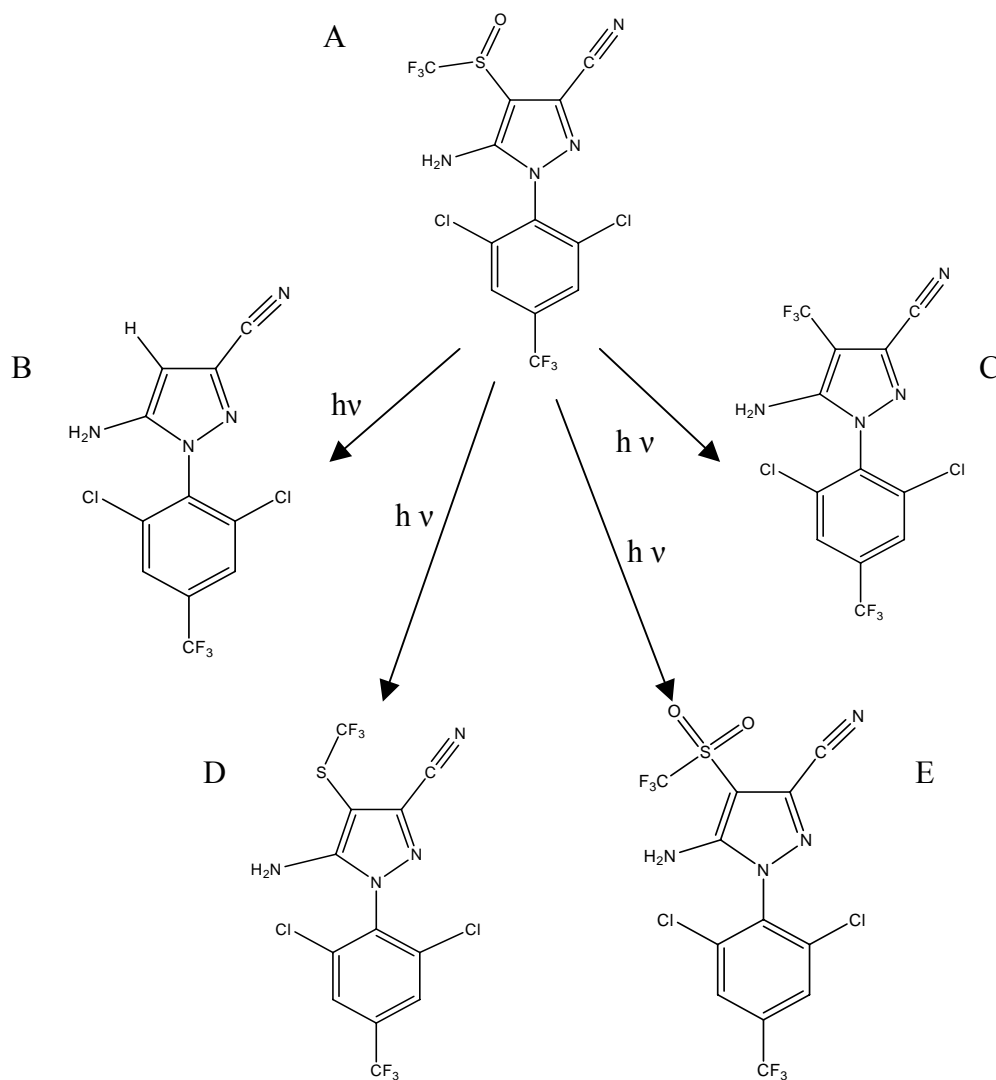


Figure 3. The photoproducts of fipronil (A) under environmental conditions; fipronil-detrifluoromethylsulfinyl (B), fipronil-desulfinyl (C), fipronil-sulfide (D), and fipronil-sulfone (E).

(Bobe et al., 1998b; Figure 4). At pH 12, fipronil hydrolytic degradation was 300 times faster than at pH 9. Temperature also influenced the hydrolytic degradation of fipronil. For example, the $t_{1/2}$ of the insecticide decreased from 114 to 18 hours as the temperature was increased from 22°C to 45°C (Bobe et al., 1998a). The suggested reaction mechanism involves nucleophilic

addition of the hydroxyl ion to the polar nitrile bond of fipronil (Figure 4). The $t_{1/2}$ of fipronil-amide by hydrolysis took 542 hours at pH 9 (Ngim and Crosby, 2001).

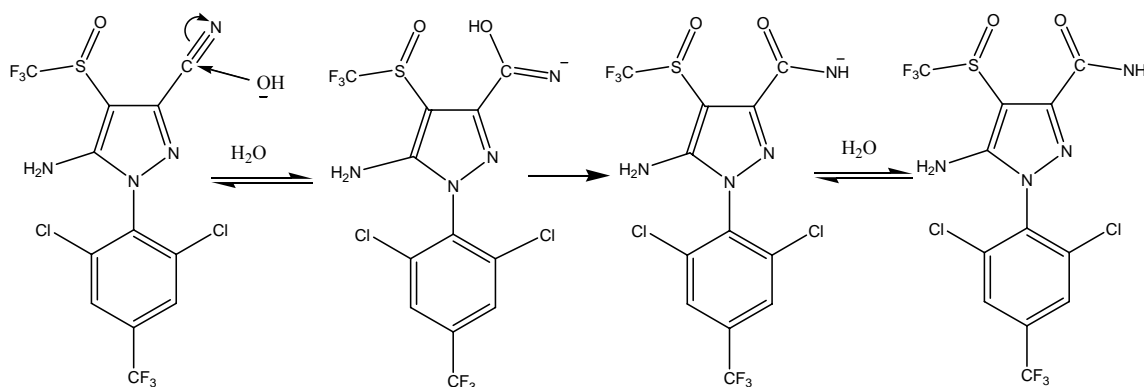


Figure 4. Hydrolysis reaction mechanism of fipronil in alkaline solution (Bobe et al., 1998b).

This data shows that hydrolysis may not be the major degradative pathway for fipronil since it is stable at typical environmental pH's.

D. Biotic

The microbial degradation of fipronil in soils was studied by Zhu et al. (2004) who found that $t_{1/2}$ of fipronil in non-sterile clay loam soil was 9.72 and 8.78 days at 25°C and 35°C, respectively (Figure 2). It took three times longer (approximately 33 days) in the sterile soils. However, longer $t_{1/2}$'s have been observed; as long as 342 days in loam soil (Tingle et al., 2003). It is reported that in sandy loam soils the $t_{1/2}$ for fipronil is 126 days (Rhône-Poulenc Ag Company, 1998). Similarly, reported $t_{1/2}$ of fipronil in sandy loam was 122 days with fipronil-amide and fipronil-sulfone accounting for 27-38% and 14-24% of the total byproducts, respectively (U.S. EPA, 1996).

Anaerobic soil dissipation was found to be shorter (Ngim and Crosby, 2001) in California rice fields (Table 1); in water the $t_{1/2}$ ranged from half-day to 5 days while in soil it was longer (2-22 days). A longer $t_{1/2}$ in soil (113 days) is reported elsewhere and fipronil-sulfide was found after 365 days of incubation (Rhône-Poulenc Ag Company, 1998).

The major degradation product in soil was fipronil-sulfide (reduction) and in water fipronil-desulfinyl (photolysis; Figure 2). Fipronil-amide (hydrolysis) and fipronil-sulfone (oxidation) degradation products were also found but at low concentrations (Ngim and Crosby, 2001). The microbial degradation of fipronil-desulfinyl (major soil photoproduct) has also been studied (Rhône-Poulenc Ag Company, 1998). Calculated $t_{1/2}$'s were 630-693 days depending on the soil. The results show that the major photolytic metabolite of fipronil is persistent in soil.

Moisture is an important factor when considering the dissipation of fipronil. The $t_{1/2}$ of fipronil was 68-198 days depending on the soil moisture content (Table 3). However, shorter $t_{1/2}$ have been reported in a study by Zhu et al. (2004). Similarly, about 14.5 days was found to be the $t_{1/2}$ for fipronil in pond water and sediment (aerobic) and the major degradation product was fipronil-sulfide (Rhône-Poulenc Ag Company, 1998). While Zhu et al. (2004) showed that temperature increases the dissipation time by about one day. Ying and Kookana (2002) found that moisture in the soil determined the type of degradation product that forms. For instance, soil with more than 50% moisture tended to have more fipronil-sulfide; result of the reduction pathway since high moisture promotes a reduced environment due to the lack of aeration. In contrast, soils with good aeration and less than 50% moisture had more fipronil-sulfone (Ying and Kookana, 2002). In both studies, the sterile soils had much longer dissipation times as compared to the non-sterile soils (Table 3).

Bacteria, fungi, and actinomycetes populations, as measured by plate counts, revealed no consistent pattern with fipronil concentration; the populations varied throughout the incubation period (Zhu et al., 2004).

Table 3. Fipronil half-lives ($t_{1/2}$) from laboratory and field studies.

Soil and condition	$t_{1/2}$ (days)
<i>Field</i>	
High treatment plot (application rate of 0.15 g/m ²) ¹	139
Low treatment plot (application rate of 0.075 g/m ²) ¹	124
<i>Laboratory</i>	
Sandy loam sterile with 15% maximum water holding capacity ¹	217
Sandy loam sterile with 60% maximum water holding capacity ¹	210
Sandy loam non-sterile with 15% maximum water holding capacity ¹	198
Sandy loam non-sterile with 30% maximum water holding capacity ¹	161
Sandy loam non-sterile with 60% maximum water holding capacity ¹	68
Clay loam sterile at 25°C ²	33.5
Clay loam sterile at 35°C ²	32.1
Clay loam non-sterile at 25°C ²	9.72
Clay loam non-sterile at 35°C ²	8.78

¹ Ying and Kookana, 2002; ² Zhu et al., 2004;

V. Toxicity

A. Direct

1. Insects

Fipronil, as an insecticide, is highly effective against mosquito larvae (*Culex quinquefasciatus*), according to Ali et al. (1999). The reported LC₉₀ was 0.90 µg/L while the LC₅₀ was 0.35 µg/L. Its toxicity to *Aedes aegypti* mosquito larvae produced 24 hour and 48 hour LC₅₀'s of 24.8 nM (~11.7 µg/L) and 15.1 nM (~7.14 µg/L), respectively (Aajoud et al., 2003). The degradation products are also highly toxic to *Aedes aegypti* larvae; LC₅₀ for fipronil-sulfide

and fipronil-sulfone was 8.8 nM (~3.79 µg/L; Aajoud et al., 2003; Figure 2). Steven et al. (1998) found that fipronil is highly toxic to insect fly midges (*Chironomus tepperi*) that are found, as pests, in rice fields at very low concentrations; LC₅₀ and LC₉₀ is 0.43 and 1.05 µg/L, respectively. Ali et al. (1998) observed almost the same LC₅₀ for the midges fly. Table 4 summarizes data from several studies on the toxicity of fipronil to various insects.

Table 4. The toxicity of fipronil to various insects in µg/L unless specified.

Insect	Species	Test	Amount (µg/L)
Mosquito ¹	<i>Aedes aegypti</i>	LC ₅₀	1.54
Mosquito ¹	<i>Aedes albopictus</i>	LC ₅₀	23.0
Mosquito ¹	<i>Aedes taeniorhynchus</i>	LC ₅₀	0.43
Mosquito ¹	<i>Culex nigripalpus</i>	LC ₅₀	0.87
Mosquito ¹	<i>Culex quinquefasciatus</i>	LC ₅₀	0.35
Midges ¹	<i>Chironomus crassicaudatus</i>	LC ₅₀	0.42
Midges ¹	<i>Glyptotendipes paripes</i>	LC ₅₀	0.42
Honeybee ²	<i>Apis mellifera</i>	LD ₅₀	4-6.2 ng/bee
Honeybee ³	<i>Apis mellifera</i>	LD ₅₀	<5 ng/bee
Boll weevil ⁴	<i>Anthonomus grandis grandis</i>	48 hourLD ₅₀	0.040 µg/weevil
Boll weevil ⁴	<i>Anthonomus grandis grandis</i>	72 hourLD ₅₀	0.029 µg/weevil
German cockroach ⁵	<i>Blattella germanica</i>	LD ₅₀	4.6-5.4 ng/cockroach

¹ Ali et al., 1998; ² Tingle et al., 2003 and Decourtye et al., 2002; ³ Hassini et al., 2005;

⁴ Mulrooney and Goli, 1999; ⁵ Valles et al., 1997.

Low concentrations have also been shown to control the onion maggot, *Delia antiqua*. Fipronil at 25 µg/mg seed, controlled the onion maggot population with only about 4% seed loss (Nault et al., 2006). Fipronil is additionally highly toxic to the boll weevil (Table 4) and a residue as low as 3 ng/cm² which, on leaves killed about 48% of the boll weevil's exposed to the insecticide (Mulrooney and Goli, 1999). The red fire ant (Hymenoptera: formicidae) is another insect highly sensitive to fipronil with granular baits containing 3-30 µg/mg eliminating colonies in 8-11 weeks after treatment (Collins and Callcott, 1998). A corresponding field trial by the same authors showed that 15 µg/mg granular bait provided over 80% colony mortality at 6 and

12 weeks after application. Costa and Rust (1998) have also examined the mortality rates of ant (Argentine) colonies with fipronil and found mortality rate $\geq 93\%$ in as little as one week. Queen ants were killed within 4 weeks after exposure to fipronil (Costa and Rust, 1998). Like ants that live in the soil, termites are also affected by fipronil. For example, Hu (2005) studied the efficacy of fipronil on termite populations: *Reticulitermes flavipes* and *Coptotermes formosanus*. Exposed soils were monitored for tunneling depth and insect mortality. The termites tunneled 87 ± 0.21 and $47 \pm 0.18\%$ deep in the 50 mm soil with 50 and 100 mg/L fipronil, respectively, before dying. Fipronil is observed to be a non-repellent pesticide that can retard the activity of the termites before death (Hu, 2005).

At concentrations approximately an order of magnitude below the LC_{50} , Hassani et al. (2005) reported that fipronil did not interfere with locomotive activity of honeybees regardless of whether the route of administration was topical (0.1 and 0.5 ng/bee) or oral (0.5 ng/bee). The study further examined the effects of fipronil on honeybee sucrose activity since sucrose is essential to making foraging decisions and organizing the division of hive labor (Pankiw and Page, 1999; Hassani et al., 2005). Orally absorbed fipronil had no significant effect on sucrose activity at the 0.5 ng/bee concentration. Further, fipronil induced no significant impairment of learning and memory retention performance; however, the concentration of 0.5 ng/bee impaired the olfactory learning of the honeybees (Hassani et al., 2005). The LD_{50} of fipronil to the honeybee is only 4 ng/bee (Tingle et al., 2003) to 6.2 ng/bee (Decourtye et al., 2002).

Balança and Visscher (1997) found that very low doses of fipronil (i.e., 0.6 g a.i./ha) can effectively control a grasshopper outbreak. One to 2 g/ha resulted in high mortality rates with more than 90% of the insects disappearing within 3-10 days. An increase in mortality in a shorter time was achieved with higher doses (Balança and Visscher, 1997).

In contrast to the above insect findings, Pino and Jove (2005) found that fipronil had a “negligible” effect on three nematode species in consideration to the concentration used (250 mg/L) and applied field rate (12-60 mg/L). The findings are based on the results that 2000 mg/L fipronil exposure for 72 hours resulted in only 17% mortality for *Heterorhabditis bacteriophora*. However, although similar results were obtained for the nematode *Steinernema carpocapsae*, high mortality rates (100%) were observed for *Steinernema arenarium* species (Pino and Jove, 2005). This high rate is about 33 times greater than the highest field application rate of 60 mg/L.

The degradation products of fipronil were also found to have strong insecticidal properties; fipronil-desulfinyl and fipronil-amide had LC₅₀'s of 62.7nM (29.7 µg/L) and 121.6 nM (57.5 µg/L), while it was 8.8 nM (3.79 µg/L) for fipronil-sulfide and fipronil-sulfone, respectively to the larvae of *Aedes aegypti* mosquito (Aajoud et al., 2003). In a similar study with the boll weevil, the 48-hour LD₅₀ of fipronil, fipronil-desulfinyl, fipronil-sulfone, and fipronil-sulfide was 0.040, 0.174, 0.068 and 0.035 µg/weevil, respectively. At 72 hours, the LD₅₀ was lower for the same degradation products: 0.029, 0.126, 0.031 and 0.020 µg/weevil (Mulrooney and Goli, 1999). The sulfone degradation product also binds to GABA receptors like its parent compound (Aajoud et al., 2003). The photoproduct, desulfinyl-fipronil, is toxic to both houseflies and mice; LD₅₀ for housefly was 0.13 and 0.058 mg/kg for fipronil and fipronil-desulfinyl, respectively, while it was 41 and 23 mg/kg for the mouse (Hainzl and Casida, 1996).

2. Aquatic organisms

Fipronil is highly toxic to many aquatic species (U.S. EPA, 1996) and bio-accumulates in some. For instance, ppt (ng/L) levels of fipronil affect Mysid shrimp and ppb (µg/L) levels affected freshwater *Daphnia* and Bluegill sunfish (Table 5). Stark and Vargas (2005) determined that only certain concentrations, those approaching the LC₅₀, can negatively affect population

parameters, such as reproductive rate, birth rate, death rate, and doubling time, of the water flea, *D. pulex* (Table 5). The LC₅₀ for *D. pulex* was about 16 µg/L (relatively toxic) according to the same study. Other important finding from the study were that increased fipronil concentrations led to a decline in the population growth rate of the water flea and population extinction (negative growth rate) was observed at 80 µg/L concentrations.

Ngim and Crosby (2001) found fipronil to be toxic to crayfish that live in rice fields at ppb levels: 14.3–19.5 µg/L (Table 5). Further, its degradation products have been found to have similar or greater toxicity - the 96 hour LC₅₀'s for fipronil-sulfone, fipronil-sulfide, and fipronil-desulfinyl were on average 11.2, 15.5, and 68.6 µg/L, respectively to crayfish (Schlenk et al., 2001). Fipronil-sulfone and sulfide LC₅₀'s were similar or lower than that of fipronil (11.1-14.3 µg/L). To the bluegill sunfish, fipronil-sulfone has been found to be 3.3 times more toxic while the same degradation product and sulfide byproduct are 6.6 and 1.9 times more toxic, respectively, to fresh water invertebrates than the parent compound (Demcheck and Skrobialowski, 2003). Mesléard et al. (2005) found large differences in invertebrate families in rice fields under conventional (use of insecticides) and organic agriculture practices (no pesticides). Fipronil was found to be one of the main factors that could explain these differences and thus, had a negative impact on predatory invertebrates.

Exposure of *Daphnia pulex* to 30 µg/L was found to affect reproduction (Stark and Vargas, 2005). In a more detailed study to better understand the fipronil toxicity, Konwick et al. (2005) researched the acute enantioselective toxicity of fipronil, the racemate, and desulfinyl derivative on the insect invertebrate, *Ceriodaphnia dubia*. Enantiomers have the same abiotic degradation and physical-chemical properties but different biological activity, microbial degradation rates, and toxicity. The 48 hour LC₅₀ for the (+) enantiomer was 10.3 ±1.1 µg/L

while it was 31.9 ± 2.2 $\mu\text{g/L}$ for the (-) enantiomer. The racemate (mixture) LC_{50} was 17.7 ± 1.3 $\mu\text{g/L}$. This information shows that the (-) enantiomer has lower impacts on *Ceriodaphnia dubia* insects (Konwick et al., 2005).

Table 5. Toxicity of fipronil to aquatic animals in $\mu\text{g/L}$ unless specified.

Animal	Test	Amount ($\mu\text{g/L}$)
Oysters *	EC_{50}	770
Mysid shrimp *	EC_{50}	140 ng/L
Sheephead minnow *	EC_{50}	130
Daphnia *	EC_{50}	190
Bluegill sunfish *	96 hour LC_{50}	83.0
Rainbow trout *	96 hour LC_{50}	250
Crayfish (red swamp) ¹	96 hour LC_{50}	14.3
Crayfish (while river) ¹	96 hour LC_{50}	19.5
<i>Ceriodaphnia (dubia)</i> ²	48 hour LC_{50}	17.7
<i>Daphnia (pulex)</i> ³	LC_{50}	9-83
<i>Ceriodaphnia (dubia)</i> ²	48 hour LC_{50} [(+) enantiomer]	10.3
	48 hour LC_{50} [(-) enantiomer]	31.9

* U.S. EPA, 1996; ¹ Schlenk et al., 2001; ² Konwick et al., 2005; ³ Stark and Vargas, 2005.

Low concentrations of fipronil's degradation products have also been found to be toxic to aquatic organisms and hinder reproduction (Table 6; Rhône-Poulenc Ag Company, 1998). The extreme toxicity of, for example, fipronil sulfone is clearly evident since only 4.5 ppb ($\mu\text{g/L}$) affects *Daphnia magna*, a benchmark aquatic organism.

Table 6. Toxicity of fipronil's degradation products to aquatic animals in $\mu\text{g/L}$ unless specified.

Aquatic organisms	Test	Metabolite concentration		
		Fipronil-desulfinyl	Fipronil-sulfone	Fipronil-sulfide
Bluegill sunfish	96 hour LC_{50}	20	25	-
Rainbow trout	96 hour LC_{50}	31	39	-
<i>Daphnia magna</i>	21 day EC_{50}	230	4.5	27
<i>Daphnia magna</i>	48 day EC_{50}	-	29	100
Mallard duck	LC_{50}	437 mg/kg	-	-

3. Birds

Fipronil has been found to be toxic to land game birds on an acute oral and sub-acute dietary basis, but not very toxic to some waterfowl (U.S. EPA, 1996). Low toxicity to some birds was noted by Avery et al. (1998) where mallard duck, pigeon, and field sparrow had LD₅₀'s of was 2150, >2000, and 1120 mg/kg, respectively, while the LD₅₀ for the Northern bobwhite quail was 11.3 mg/kg.

B. Indirect

Very low doses of fipronil, applied to control grasshoppers, had an impact on non-target insects, specifically Coleoptera, Hymenoptera, and Diptera (Balança and del Visscher, 1997). Dosages of 1 and 2 g a.i./ha was found to increase mortality rates of grasshoppers while having reduced consequences to non-target insects such as beetles as compared to higher doses (Balança and del Visscher, 1997). These beetles are of agricultural importance because they can contribute to biological pest control.

Mesléard et al. (2005) found that fipronil had an indirect effect on heron diet. More herons were observed foraging for insects in organic (no fipronil treatments) rice fields when compared to fipronil treated plots. This difference was attributed to a reduction in the invertebrates and their larvae that contribute to the heron diet in the fipronil treated rice fields. For instance, 30 and 22 invertebrate families were found in untreated (organic) and treated plots, respectively (Mesléard et al., 2005). In contrast, fipronil did not negatively affect birds that consumed fipronil-treated rice seeds (Avery et al., 1998). In a controlled caged experiment, fipronil treated seed was fed to the red-winged blackbird (*Agelaius phoeniceus*), brown-headed cowbirds (*Molothrus ater*), and boat-tailed grackles (*Quiscalus major*) and the results showed

that 325-500 mg/kg fipronil applications alone to rice fields do not affect avian feeding activity (Avery et al., 1998).

C. Antagonistic toxicity

The effectiveness of fipronil toxicity was antagonized by S,S,S,-tributyl phosphorotrithioate (DEF) and piperonyl butoxide (PBO) on the German cockroach, *Blattella germanica* (Valles et al., 1997). Fipronil was about 2.3-3.0 times less toxic to cockroaches pretreated with PBO and similar results was obtained for DEF. Overall, the study by Valles et al. (1997) found that fipronil is activated metabolically in the cockroaches and may form fipronil-sulfone as its metabolite (Valles et al., 1997).

VI. Summary

Fipronil is phenylpyrazole insecticide that exhibits neuro-toxic activity by blocking the GABA-regulated chloride channels of neurons. It is useful for the control of many domestic and agricultural insect pests and formulated as a bait, spray, and granular product. Overall, the dissipation of fipronil exhibits low to moderate persistence and can be explained by a combination of photolysis, hydrolysis, sorption, and volatilization processes. There are five degradation products depending on the mode of dissipation; fipronil-sulfone, fipronil-sulfide, fipronil-desulfinyl, fipronil-amide, and fipronil-detrifluoromethylsulfinyl.

In soil, fipronil has low to moderate sorption which increases with greater organic matter content. Dissipation in soil is via gradual microbial breakdown; anaerobic and aerobic half-lives ($t_{1/2}$) extend from four months to one year, respectively, while on the soil surface, photolysis contributes primarily to its breakdown. Fipronil is more susceptible to breakdown through

photolysis than hydrolysis in water at typical environmental pH's and moisture content in the soil determines the type of degradation product that forms. Fipronil is unstable and readily degrades under alkaline conditions. The insecticide has been detected in California and U.S. water bodies. The detections in California most likely come from urban structural pest control uses, since the product is not registered for production agricultural uses. Due to its low vapor pressure and Henry's Law constant, fipronil is not likely to be found in the air.

Many insects (both beneficial and pests) are highly sensitive to fipronil in larval and adult stages. The major degradation products are also toxic to many insects. Very low doses of fipronil, applied to control grasshoppers, had an impact on some non-target insects. There are reports that fipronil does not interfere with locomotive activity of the honeybee but their LD₅₀ is only 4 ng/bee. Similarly, it is highly toxic to aquatic organisms. Fipronil has been found to be toxic to land game birds on an acute oral and sub-acute dietary basis, but not very toxic to some waterfowl. Care should be taken when applying this insecticide to an area adjacent to, or near, water bodies.

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